

Acta Neurochir (2010) 152:2079–2084
DOI 10.1007/s00701-010-0813-4

TECHNICAL NOTE

Diffusion tensor imaging (DTI) and colored fractional anisotropy (FA) mapping of the subthalamic nucleus (STN) and the globus pallidus interna (GPi)

Mark Sedrak · Alessandra Gorgulho · Ausaf Bari ·
Eric Behnke · Andrew Frew · Inga Gevorkyan ·
Nader Pouratian · Antonio DeSalles

Received: 10 August 2010 / Accepted: 16 September 2010 / Published online: 3 October 2010
© The Author(s) 2010. This article is published with open access at Springerlink.com

Abstract

Introduction The subthalamic nucleus (STN) and the globus pallidus internus (GPi) are the most common surgical targets for the treatment of Parkinson's disease. We studied directionally colored fractional anisotropy (FA) and diffusion tensor imaging (DTI) sequences to better target these anatomical regions.

Methods Four patients undergoing stereotactic surgery for movement disorders were studied. Stereotactic targets and fiber tractography were determined on MRIs using the Schaltenbrand–Wahren atlas for definition in the iPlan software. In addition, post-operative imaging was fused to preoperative FA sequences for end-result identification. Axial, sagittal, and coronal images of the FA sequence were studied. DTI parameters used ranged from 2 to 4 mm for voxel size in the $x/y/z$ planes, fiber length was kept constant at 15 mm and FA threshold of 0.25.

Results Colored FA maps resulted in a key signature in and around the STN and GPi. Regions identified include, but were not limited to: the internal capsule, nigral projections,

the thalamic fasciculus, Forel's fields H1 and H2, zona incerta, subthalamic fasciculus, tegmental tracts, and cerebello-rubro-thalamic tract.

Conclusions Colored FA maps allow a potential method to identify the STN and GPi accurately. DTI has proven to be a powerful tool that can be used to augment identification of the STN nucleus and GPi used for stereotactic surgery.

Keywords Deep brain stimulation · Diffusion tensor imaging · Fiber tractography · Subthalamic nucleus · STN · Globus pallidus · Pars interna

Introduction

The subthalamic nucleus (STN) and globus pallidus interna (GPi) have received much attention in the treatment of movement disorders because of their efficacious effects during surgical treatment [3]. The STN and the GPi, on many magnetic resonance imaging (MRI) sequences can be ill defined and microelectrode recordings during the surgical placement are necessary for precise targeting [11, 14]. In addition, stimulation of the region is often necessary intraoperatively not only for evaluation of efficacy, but also for evaluation of limiting side-effects.

The application of diffusion tensor magnetic resonance imaging has enhanced the ability to view anatomical detail beyond what is seen by conventional MRI or computed tomography (CT) scans. Indeed, diffusion tensor imaging (DTI) allows in vivo imaging of fiber tracts in humans [1, 9, 10, 12]. The fractional anisotropic (FA) maps are typically processed for tractography purposes. In this study, we studied these “raw” FA images for their anatomic information to better identify the STN and GPi nuclei.

M. Sedrak · A. Gorgulho · A. Bari · E. Behnke · I. Gevorkyan ·
N. Pouratian · A. DeSalles
Department of Neurosurgery, David Geffen School of Medicine,
University of California Los Angeles (UCLA),
Los Angeles, CA 90095, USA

A. Frew · I. Gevorkyan
Department of Neurology, David Geffen School of Medicine,
University of California Los Angeles (UCLA),
Los Angeles, CA 90095, USA

M. Sedrak (✉)
The Institute of Brain and Spine Surgery,
21350 Hawthorne Blvd., Suite 176,
Torrance, CA 90503, USA
e-mail: msedrak@gmail.com

These FA sequences can be colored based on fiber directionality. We theorized that this enhanced imaging would help us better identify the necessary anatomy required for optimal targeting.

Methods

Of 392 patients who have undergone deep brain stimulation (DBS) from November 18, 1993 to February 18, 2010, we retrospectively reviewed four MRI image sets of patients who underwent DBS for Parkinson's disease, two with bilateral GPi and two with bilateral STN. One of these patients had DTI performed in the 1.5 Tesla Sonata intraoperative MRI (iMRI) suite and the other three had 3.0 Tesla MRI. We also selected patients who had improvement of their symptoms during intraoperative stimulation, had no significant side-effects on initial placement of electrode with stimulation, and good follow-up results. Of the eight electrodes placed, one electrode targeting posteroventral GPi was moved 4 mm lateral because of motor side effects.

Diffusion tensor, T1, T2, fluid-attenuated inversion recovery (FLAIR) source imaging acquisition was undertaken either preoperatively or intraoperatively before placement of the Leksell stereotactic frame. The Leksell frame was placed parallel to Reid's line under sedation. The one patient who had 1.5 Tesla imaging performed was then rescanned in the Sonata iMRI suite for frame registration. The patients with the 3.0 Tesla preoperative MRI were rescanned with the Leksell frame in place with intraoperative CT. All stereotactic planning was performed on BrainLAB's iStereotaxy 2.6.

The technique of surgery for the STN/GPi target was standard. After standard sterilization and opening, the patient was awakened and a microelectrode was used to target the nucleus depth. After this, the Medtronic 3389 electrode was placed for STN and Medtronic 3387 was used for GPi. Trial stimulation was then performed with Medtronic 3628 stimulator at a frequency of 160 Hz (STN), 130 Hz (GPi) and a pulse width of 90 ms. After adequate clinical response and appropriate placement, the electrode was secured using a Navigus cap (Image Guided Technologies, Inc., Boulder, CO, USA). Post-operative CT or MRI was performed to check placement of the leads. The implantable pulse generators were implanted at a later stage, typically about 2 weeks post-operatively. A detailed description of the stereotactic procedure as well as the imaging acquisition for targeting has been previously reported [2, 6].

One patient had 12-directional DTIs performed before frame placement with 1.5T MRI. DTI data was acquired using single-shot spin-echo echo-planar imaging with TR=10,000 ms, TE=90 ms, acquisition matrix=128×128 and field of view=25.6 cm. Slice thickness of 2 mm with no

gap was used. Diffusion-sensitizing gradient encoding was applied in 12 directions by using a diffusion-weighted factor $b=700$ s/mm², and one image was acquired without use of a diffusion gradient, i.e., $b=0$ s/mm². The DTI imaging time was approximately 4 min.

Three patients had 3.0T MRI performed, which were 20-directional DTIs performed before placement of the frame. DTI data was acquired using single-shot spin-echo echo-planar imaging with TR=9,100, TE=87 ms, acquisition matrix=128×128 and field of view=25.6 cm. Slice thickness of 2 mm with no gap was used. Diffusion-sensitizing gradient encoding was applied in 12 directions by using a diffusion-weighted factor $b=1000$ s/mm², and one image was acquired without use of a diffusion gradient, i.e., $b=0$ s/mm². The DTI imaging time was approximately 3:40 min.

BrainLab's iPlan Cranial 2.6, Stereotaxy 2.6, or RT 4.1 software was used in all the analyses. Eddy current correction was used in all patients. Colored FA maps were used to identify the STN/GPi nucleus and surrounding structures using the Schaltenbrand–Wahren atlas information and MRI sequences such as T1, T2, SPGR, and FLAIR. Final electrode placement was analyzed post-operatively and final trajectories were traced based on artifact location using post-operative MR scans [2]. All images were automatically fused and manually checked to confirm appropriate fusion using the software. The STN/GPi nucleus as defined by the FA map was then compared to the STN/GPi nucleus as defined by atlas and compared to the final electrode position.

Axial, coronal, and sagittal images of the colored FA map were analyzed for identification of consistent anatomy and structures across patients. A standard color scheme was used in the BrainLAB software to encode the FA maps, with blue indicating superior–inferior, red indicating transverse, and green indicating anterior–posterior. When key characteristics were identified, they were marked using the object creation tool. Anatomic correlation between these regions was then studied with the atlas as well as other MRI images. Fiber tractography was finally used in key regions of interest to better understand and demonstrate the anatomy and connectivity of the region.

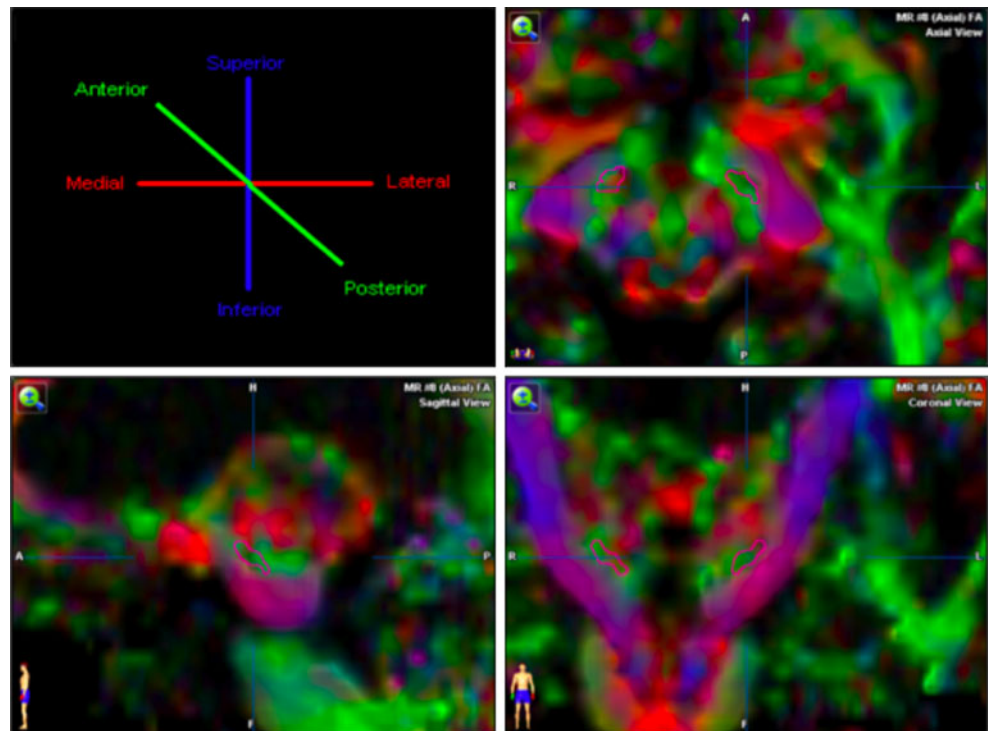
Results

Consistent patterns in colored FA map across all patients improved visualization and identification of key anatomy in the region of both the STN and the GPi.

Subthalamic nucleus and region

Major white matter bundles were also visible and clearly distinguishable even when they were not readily definable

Fig. 1 Data displaying color map based on FA sequences. Colors indicate direction of fiber tracts (*red* transverse, *blue* cranio-caudal, *green* anterior–posterior). Axial, sagittal, and coronal views are shown. *Red outline* demonstrates location of STN based on Schaltenbrand–Wahren atlas



on T1- and T2-weighted imaging especially in the subthalamic region. The subthalamic nucleus could be identified in the corner of the bundle of fibers with nigral projections (Fig. 1). An unmistakable region of interest is the posterior limb of the internal capsule (PLIC) because of its large segment consistently contains a fairly homogenous color.

The subthalamic region contained a consistent finding of distinguishable tracts (Fig. 2). One of these tracts was the internal capsule, which was most lateral on coronal imaging. Immediately superior and medial to the internal capsule was a region with fibers in an anterior–posterior direction presumably containing many nigral projections. The tract superior to this just below the thalamus was

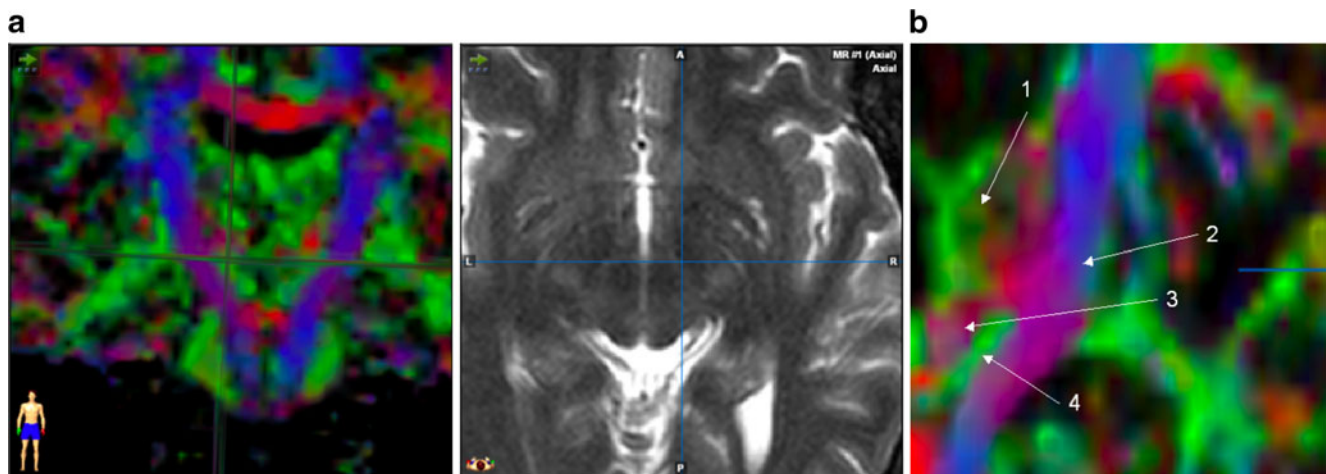


Fig. 2 **a** Coronal imaging of FA map demonstrated a consistent finding correlating with efficacious post-operative DBS insertion. The region contains fiber bundles with different directionality exemplified by the color differentiation in the subthalamic region. Cross-hairs demonstrate STN as target. The coronal FA map also contained a region connecting the upper fibers with the internal capsule which is nearly parallel to the AC–PC line and typically where the tip of the DBS would lie. Actual final electrode stereotactic trajectory placed on

coronal FA Map. **b** Higher magnification view of coronal FA Map. *1* Thalamus. Note heterogeneity of color coding. *2* Note posterior limb of the internal capsule which is *purple* and *blue* in color indicating its vertical trajectory. *3* The *red* area seen below the thalamus contains the cerebello-rubro-thalamic tract, zona incerta, thalamic fasciculus. *4* The *green* area below this contains the subthalamic nucleus in its corner, but also contains the subthalamic fasciculus and nigral projections

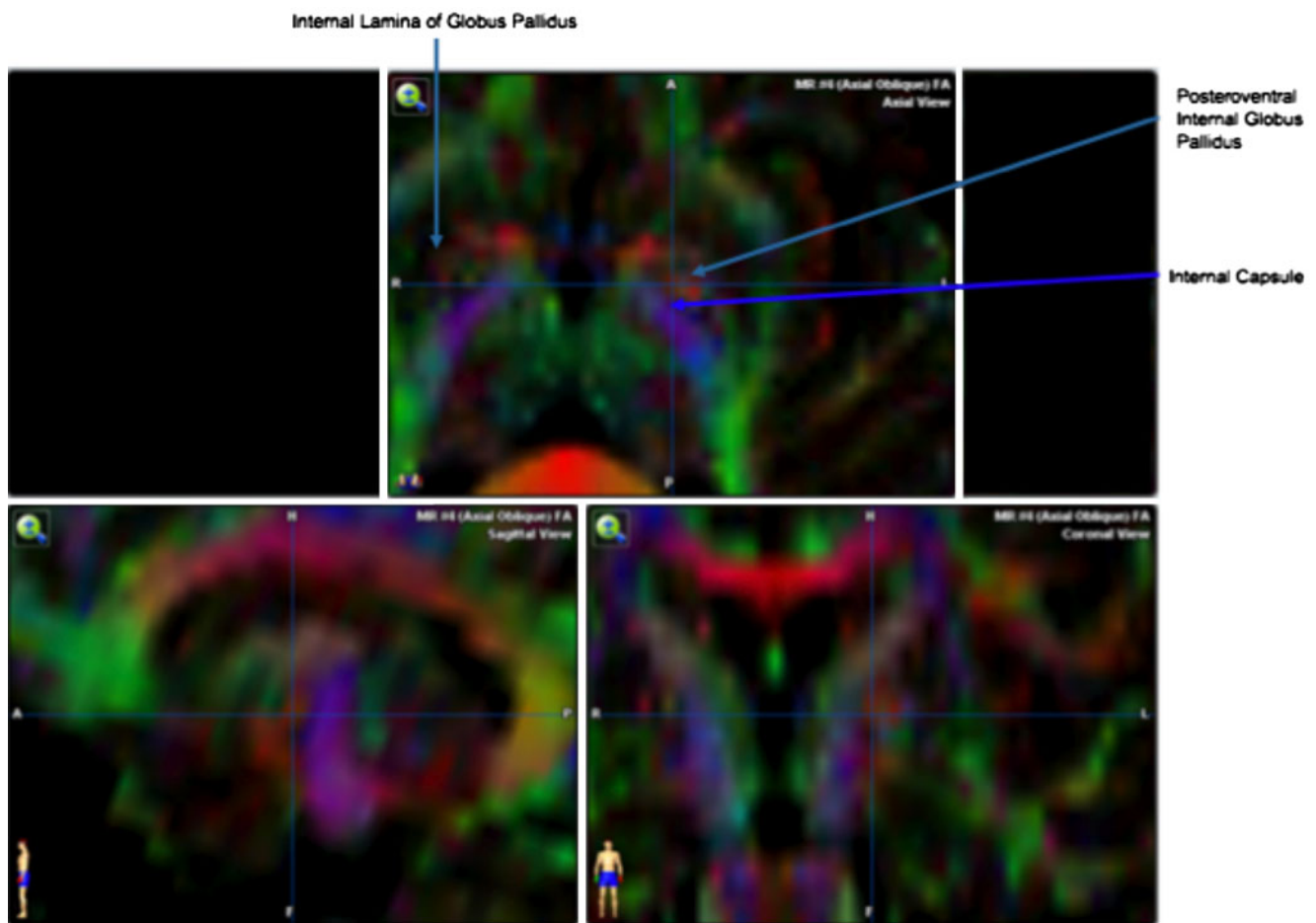


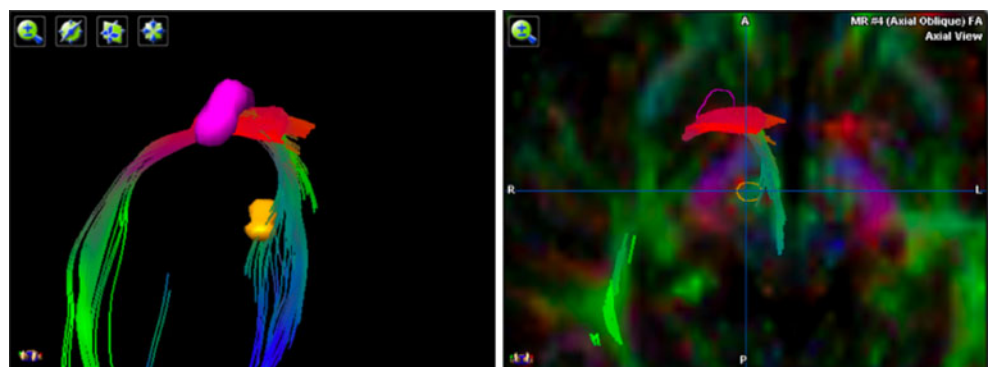
Fig. 3 GPi, 3 T MRI. Posteroventral GPi. External and internal lamina of GP are present. The heterogeneity seen in the globus pallidus and putamen are appreciated and their borders distinguished by *white matter tracts*

typically transverse in direction (i.e., red) and contained cerebello-rubro-thalamic tracts, lemniscal fibers, fibers of the thalamic fasciculus and Forel's fields. This most superior tract also typically included a band projecting laterally to the internal capsule; this intersection also contained the zona incerta and was at the intercommissural plane.

Globus pallidus and region

Colored FA maps highlighted boundaries between major gray and white matter regions, which can sometimes be obscured on T1- or T2-weighted imaging. The boundaries between the posterior limb of the internal capsule, the thalamus, and the globus pallidus could be unambiguously

Fig. 4 DTI Imaging of the Pallidum and Subthalamic Region. *Purple* is pallidum, *gold* is STN. Fibers can be seen traversing portions of the subthalamic nucleus and the globus pallidus. Interconnectivity is seen (FA 0.25 and Min fiber length 15 mm)



delineated using color FA maps (Fig. 3). Major white matter tracts helped in this delineation because of their confluent color. For example, the PLIC was mostly blue in color. Conversely, regions such as the thalamus or globus pallidus containing grey matter developed heterogeneity of color with regional variation.

Diffusion tractography

Region of interest (ROI) was placed in the STN/GPI nucleus as identified by the Schaltenbrand–Wahren atlas and efficacious electrode placement. Tractography of these ROIs demonstrated fibers entering or exiting the both nuclei (Fig. 4). These fibers included the ansa lenticularis, subthalamic tracts, and Forel's field (FA 0.25 and minimum fiber length of 15 mm).

Discussion

Diffusion tensor tractography has numerous applications in neurosurgery. The raw images gathered for DTI images can be processed yielding a directionally coded colored FA map. These colored FA maps yield anatomic information when studied in detail beyond that which is gathered by conventional MRI sequences. DTI imaging has been shown beneficial in studying white matter tracts and even used for directed targeting [4, 5]. However, colored FA maps have not been used to for DBS targeting thus far. We have also noted recently that these color FA maps can be used to identify regions of grey matter anatomy, even in the thalamus. Enhancing the anatomical identification of major tracts in the subthalamic and globus pallidus regions would help with precise patient-specific targeting. Based on our study, we feel that this region was clearly identified on both 1.5 T and 3.0 T MRI, which has applicability throughout the neurosurgical community. Higher quality imaging and a variation of these techniques will likely improve further the visualization of these nuclei.

Identification of white matter tracts can be critical in reducing the side-effects common to deep brain stimulation while improving the benefits. For example, our previous study had demonstrated through clinical data that the common side effect of eye deviation during STN stimulation may be due to white matter fiber tracts being activated in the anterior limb of the internal capsule leading to the frontal eye fields [13]. Our limitation of this technique was that these exact tracts could not be individually visualized; however, their regions are identified as well as their anatomical associations. Further studies looking at probabilistic connectivity may help evaluate this further. We have identified the regions of the zona incerta, cerebello-rubro-thalamic tract, and Forel's fields in addition to the STN and

GPI nuclei with patient specific accuracy. This improved visualization of these regions will improve our understanding and guide targeting in the future.

Most deep brain stimulation techniques utilize a multi-modality assessment of the MRI sequences, such as T1-, T2-weighted, FLAIR sequences, followed by use of the atlas. The colored FA form of MRI adds another level of anatomical understanding. For many types of deep brain stimulation, microelectrode recordings are also utilized intraoperatively for precise targeting. Direct targeting of the subthalamic nucleus is also a method based on study of the MRI sequences [7]. This technique carefully takes into consideration the nucleus itself improving the stereotactic technique. However, the surrounding structures and white matter tracts may be equally important. Once the electrode is turned on, the area of activation may encompass both white and grey matter [8]. Therefore, close consideration of these structures will certainly guide the future of this neurosurgical technique.

Conflicts of interest None

Open Access This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

References

1. Basser PJ, Pajevic S, Pierpaoli C, Duda J, Aldroubi A (2000) In vivo fiber tractography using DT-MRI data. *Magn Reson Med* 44:625–632
2. De Salles AAF, Frighetto L, Behnke E, Sinha S, Tseng L, Torres R, Lee M, Cabatan-Awang C, Frysinger R (2004) Functional neurosurgery in the MRI environment. *Minim Invasive Neurosurg* 47:284–289
3. Follett KA, Weaver FM, Stern M, Hur K, Harris CL, Luo P, Marks WJ Jr, Rothlind J, Sagher O, Moy C (2010) Pallidal versus subthalamic deep-brain stimulation for Parkinson's disease. *Mass Med Soc* 362:2077
4. Gutman DA, Holtzheimer PE, Behrens TEJ, Johansen-Berg H, Mayberg HS (2009) A tractography analysis of two deep brain stimulation white matter targets for depression. *Biol Psychiatry* 65:276–282
5. Jellison BJ, Field AS, Medow J, Lazar M, Salamat MS, Alexander AL (2004) Diffusion tensor imaging of cerebral white matter: a pictorial review of physics, fiber tract anatomy, and tumor imaging patterns. *Am Soc Neuroradiology* 25:356
6. Lee MWY, De Salles AAF, Frighetto L, Torres R, Behnke E, Bronstein JM (2005) Deep brain stimulation in intraoperative MRI environment comparison of imaging techniques and electrode fixation methods. *Minim Invasive Neurosurg* 48:1–6
7. Lemaire J, Coste J, Ouchchane L, Hemm S, Derost P, Ulla M, Siadoux S, Gabrillargues J, Durif F, Chazal J (2007) MRI anatomical mapping and direct stereotactic targeting in the subthalamic region: functional and anatomical correspondence in Parkinson's disease. *Int J Comput Assist Radiol Surg* 2:75–85
8. McIntyre CC, Mori S, Sherman DL, Thakor NV, Vitek JL (2004) Electric field and stimulating influence generated by deep brain

- stimulation of the subthalamic nucleus. *Clin Neurophysiol* 115:589–595
9. Mori S, Crain BJ, Chacko VP, van Zijl PC (1999) Three-dimensional tracking of axonal projections in the brain by magnetic resonance imaging. *Ann Neurol* 45:265–269
 10. Poupon C, Clark CA, Frouin V, Regis J, Bloch I, Le Bihan D, Mangin JF (2000) Regularization of diffusion-based direction maps for the tracking of brain white matter fascicles. *Neuroimage* 12:184–195
 11. Romanelli P, Heit G, Hill B, Kraus A, Hastie T, Bront -Stewart H (2004) Microelectrode recording revealing a somatotopic body map in the subthalamic nucleus in humans with Parkinson disease. *J Neurosurg* 100:611–618
 12. Sedrak M, Gorgulho A, Salles A, Frew A, Behnke E, Ishida W, Klochkov T, Malkasian D (2008) The role of modern imaging modalities on deep brain stimulation targeting for mental illness. *Acta Neurochir Suppl* 101:3–7
 13. Shields DC, Gorgulho A, Behnke E, Malkasian D, Desalles AAF (2007) Contralateral conjugate eye deviation during deep brain stimulation of the subthalamic nucleus. *J Neurosurg* 107:37–42
 14. Starr PA, Turner RS, Rau G, Lindsey N, Heath S, Volz M, Ostrem JL, Marks WJ Jr (2006) Microelectrode-guided implantation of deep brain stimulators into the globus pallidus internus for dystonia: techniques, electrode locations, and outcomes. *J Neurosurg* 104:488–501